REMARKS

Claims 1-4, 7-9, 11, 13 and 15-19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 9, 11, 13 and 15-19 are rejected under 35 U.S.C. § 112, first paragraph, as being not enabling. Claim 1 is rejected under 35 U.S.C. § 101 as encompassing non-statutory subject matter. Claims 1-4 are rejected under 35 U.S.C. § 102(a) as being anticipated by Genbank locus AY274119, version AY27419.1 or GI:29826276. Claims 1-4, 709, 11, 13 and 15-19 are rejected under 35 U.S.C. § 102(e) as being anticipated by McSwiggen *et al.* (WO 2004/092383; hereafter "*McSwiggen*"). Claims 1 and 4 are rejected under 35 U.S.C. § 102(b) as being anticipated by Fodor *et al.* (U.S. 2001/0053519; hereafter "*Fodor*"). Claims 1, 7 and 8 are herein amended. Claims 11 and 15-19 are herein cancelled without prejudice. New claims 20-33 are herein added. No new matter has been introduced. Claims 1-4, 7-9, 13 and 20-33 are pending in the case. Consideration of the present application in view of the foregoing amendments and the remarks below is respectfully requested.

Election of Species

In the Response to Restriction Requirement ("Response") filed June 7, 2005, Applicants stated that Applicants elected Group I and further elected, with traverse, species SEQ ID NO:1. However, the undersigned has recently realized that the Response contained a clerical error. Applicants actually intended to elect SEQ ID NO:4, but the Response inadvertently recited SEQ ID NO:1 as an elected species. As disclosed in the present specification (*see*, for example, Figures 2, 3, 5 and 6), species SEQ ID NO:4 (*i.e.*, SARSi-4) is the most effective siRNA against the coronavirus and, therefore, this species is of great importance for Applicants. Applicants wish to point out that species SEQ ID NOS:1 through 6 are all derived from the regions within the replicase 1A region of SCoV and Applicants believe that searches required for the addition of SEQ ID NO:4 will not cause undue burden on the Examiner.

Accordingly, Applicants respectfully and earnestly request that SEQ ID NO:4 be included in the present examination.

Claim Rejection under 35 U.S.C. § 112

(1) Claims 1-4, 7-9, 11, 13, 15-19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Office Action states that claims 1, 18 and 19 are indefinite in reciting "a portion thereof" without limitation.

Claims 18 and 19 are herein cancelled and, therefore, the rejection with regard to claims 18 and 19 is now moot. Claim 1 is herein amended to more particularly point out and distinctly claim the subject matter. Support can be found, for example, at page 16, lines 23-24.

The Office Action further states that claim 4 is indefinite because it does not set any definite metes and bounds on the nucleic acids claimed.

Applicants believe that the amendment to claim 1, as discussed above, from which claim 4 is dependent, cures the deficiency.

The Office Action questions whether the term "a complement thereof" in claims 7, 18 and 19 means the complement of the entire recited sequence, or "a complement" encompass shorter complementary sequences.

Claim 7 is herein amended to become dependent from claim 1, which is herein amended to more particularly point out and distinctly claim the subject matter.

Claim 8 is rejected because it is not clear whether "a host cell" containing a vector is intended to encompass isolated host cells or cells in an intact organism.

Claim 8 is herein amended to recite "an isolated host cell".

Accordingly, Applicants respectfully request that all the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

(2) Claims 9, 11, 13 and 15-19 are rejected under 35 U.S.C. § 112, first paragraph, being not enabling.

Claims 11 and 15-19 are herein cancelled without prejudice. Accordingly, the rejection of these claims under 35 U.S.C. § 112, first paragraph, is now moot.

The Office Action states that the specification does not reasonably provide enablement for body-treating methods and compositions. In particular, the Office Action points out that "[s]ince the encoded oligopeptide is part of the nonstructural gene, one skilled in the art would have reason to doubt an unsupported assertion that an immune response against this oligopeptide would prevent or treat infection, or that the peptide would be ***useful*** diagnostically" (emphasis added). Furthermore, the Office Action goes on to state that "[a]pplicant's own publication on siRNAs states that 'Their clinical ***usefulness***, however, has yet to be demonstrated" (emphasis added). Applicants understand that this statement relates to claim 13.

Applicants respectfully traverse the rejection.

Firstly, although the encoded oligopeptide is part of the nonstructural gene, that is, RNA-dependent RNA polymerase, as the Office Action asserts, that fact itself does not invoke any doubt in one skilled in the art that the encoded oligopeptide is immunogenic. The methods for preparing various immunogenic formulations as well as

the methods for using such formulations are disclosed at page 22, line 27 through page 27, line 13 and, thus, the specification is fully enabling.

Secondly, the methods for preparing the pharmaceutical composition of the present invention as well as the methods for using such pharmaceutical compositions are disclosed at page 33, line 26 through page 37, line 14, and, thus, the specification is fully enabling.

Thirdly, the nucleic acid molecules of the present invention were effective in reducing SCoV viral replication in monkey kidney cells (FRhk-4 cells) (*see* Figures 2, 3A, 3B, 5 and 6A-6D).

Fourthly, the showing of efficacy of the formulation or the composition is not required to meet the enablement requirements.

Fifthly, the above statements in the Office Action appear to focus on usefulness of the present invention and therefore the rejection seems to relate to practical utility requirement under 35 U.S.C. § 101 (*see* the emphasis added in the quotes from the Office Action). In *In re Fisher*, 76 USPQ2d 1225 (Fed. Cir. 2005), the court states that "[w]e perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question. Successful in vitro testing will marshal resources and direct the expenditure of effort to further in vivo testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an in vivo utility" (citing *Cross v. Iizuka*, 753 F.2d 1040, at 1050, 224 USPQ 739 (Fed. Cir. 1985).

Accordingly, Applicants believe that the specification is fully enabling and the claim rejection under 35 U.S.C. § 112, first paragraph, should be withdrawn.

Claim Rejection under 35 U.S.C. § 101

Claim 8 is rejected under 35 U.S.C. § 101 because the claimed invention encompasses non-statutory subject matter.

Claim 8 is herein amended as discussed in the previous section.

Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be withdrawn.

Claim Rejection under 35 U.S.C. § 102

(1) Claims 1-4 are rejected under 35 U.S.C. § 102(a) as being anticipated by Genbank locus AY274119, version AY27419.1 or GI:29826276.

Claim 1 is herein amended to read, in the relevant portion, "[a]n isolated nucleic acid molecule consisting essentially of . . .." Thus, the present invention of claim 1 does not require the nucleotide sequence disclosed in the prior art, other than the specific portion recited in claim 1. And such a specific portion of the genomic sequence is not anticipated by the prior art. In this connection, Applicants respectfully submit that although any small fragment of SCoV, based on the published genomic sequence, may be used for designing siRNA, only a small portion of siRNAs (less than 1%) would be actually effective in reducing viral replication by over 50%. Thus, the disclosure of the entire genome of SCoV does not teach or even suggest that the specific portion represented by SEQ ID NO:1 can reduce viral replication by over 50% (*see* Figure 3A of the present specification).

Accordingly, the rejection of claim 1 as well as its directly or indirectly dependent claims 2-4 under 35 U.S.C. § 102(a) as being anticipated by Genbank locus AY274119, version AY27419.1 or GI:29826276, should be withdrawn.

(2) Claims 1-4, 7-9, 11, 13 and 15-19 are rejected under 35 U.S.C. § 102(e) as being anticipated by *McSwiggen*.

Specifically, the Office Action states that *McSwiggen* teaches a short interfering nucleic acid comprising any contiguous SARS sequence of about 19-25 contiguous bases, teaches addition of two 3' terminal deoxythymidine residues, *etc.*, and also explicitly teaches double-stranded siRNAs which comprise a portion of SEQ ID NO:1 (*i.e.*, SEQ ID NOS:43, 44, 1694 and 1695 of *McSwiggen*).

Applicants respectfully traverse the rejection.

Claims 11 and 15-19 are herein cancelled without prejudice and, therefore, the rejection is moot with regard to these claims.

With regard to the rejection of claims 1-4, 7-9 and 13, as stated in the previous section, Applicants submit that any small fragment of SCoV may be used for designing siRNA, but only a small portion of siRNAs (less than 1%) would be actually effective in reducing viral replication by over 50%. *McSwiggen* systemically divides the genomic sequence into about ***3,400 sequences*** of 19-23 nucleotides in length and simply lists them as the sequences that ***could*** be siRNAs with ***possible efficacies***. *McSwiggen* does not disclose at all which sequences out of 3,400 sequences are actually effective as siRNAs. One skilled in the art is left with choices of about 3,400 sequences to test the efficacy thereof, resulting in undue experimentation. Thus, *McSwiggen* is not enabling to be qualified as prior art.

Accordingly, Applicants respectfully request that the rejection of claims 1-4, 7-9 and 13 under 35 U.S.C. § 102(e) as being anticipated by *McSwiggen* be withdrawn.

(3) Claims 1-4 are rejected under 35 U.S.C. § 102(b) as being anticipated by *Fodor*.

Specifically, the Office Action states that *Fodor* teaches the formation of an array which comprises every single 10-mer (Example 2, at page 12).

Applicants respectfully traverses the rejection.

Although *Fodor* discloses all possible 10-mers of nucleotides, it does not teach or even suggest any specific sequences of the present invention, that is, the siRNA sequences that have efficacies in reducing SCoV viral replication by over 50%. Thus, claims 1-4 are not anticipated by or not even obvious over *Fodor*.

Accordingly, Applicants respectfully request the rejection under 35 U.S.C. § 102(e) as being anticipated by *Fodor* be withdrawn.

New Claims 20-33

New claims 20-33 correspond to claims 1-19, respectively, of the originally filed claims, except that the claims are directed to SEQ ID NO:4. No new matter has been introduced. Applicants respectfully request that the new claims be examined in the present application.

No fee is believed to be due for this submission. Should any fee(s) be required, please charge such fee(s) to Deposit Account No. 50-2215.

Dated: November 14, 2005

Respectfully submitted,

By_____

Charles E. Miller
Registration No.: 24,576
DICKSTEIN SHAPIRO MORIN & OSHINSKY LLP
1177 Avenue of the Americas
New York, New York 10036-2714
(212) 835-1400
Attorney for Applicants

CEM/IY/mgs